REMARKS

I. STATUS OF CLAIMS

Claims 1, 4, and 16 have been amended. New claims 20 and 21 have been added. Written support for the amendments can be found in the original claims and as-filed specification, as explained below. No new matter has been introduced.

Claims 1-7, 16-18, 20, 21 are currently pending.

II. ALLOWABLE SUBJECT MATTER AND CLAIM OBJECTION

Applicant thanks the Examiner for his indication of allowable subject matter in claims 4 and 5. Office Action at 18.

Claim 4 has been amended to incorporate all of the features of independent claim 1 and convert the claim into independent form. Accordingly, Applicant requests withdrawal of the objection to claims 4 and 5. Claim 4, as amended, and its dependent claim 5 thus should be allowable.

New claim 20 incorporates all of the features of independent claim 16 and recites the DNA sequence shown in SEQ ID NO: 3, the allowable subject matter as indicated in the Office Action at 9 and 18. New claim 21 depends from new claim 20 and recites the DNA sequence shown in SEQ ID NO: 4, the allowable subject matter as indicated in the Office Action at 9 and 18. Written support for the new claims can be found in the as-filed specification, e.g., paragraphs [0007], [0011], [0040]-[0042]. New claims 20 and 21 also should be allowable.

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Office Action rejected claims 1-3, 6, 7, and 16-18 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Specifically, the Office Action alleged

that the term "lactate dehydrogenase gene" recited in claims 1 and 16 is not clear "because a gene includes both the coding sequence and its promoter." Office Action at 16.

Applicant has amended independent claims 1 and 16 to replace the term "lactate dehydrogenase gene" with "lactate dehydrogenase gene coding sequence," as suggested by the Office Action at 16, thereby improving clarity.

In addition, Applicant provides the following non-limiting remarks regarding the term "lactate dehydrogenase gene." Claim 1 positively recites the "lactate dehydrogenase gene" as "[encoding] a foreign protein having lactate dehydrogenase activity" and indicates that the lactate dehydrogenase gene is "under the control of a genomic pyruvate decarboxylase promoter." Claim 16 recites similar claim language. Considering claims 1 and 16 as a whole, it would be clear to one of ordinary skill in the art that the lactate dehydrogenase promoter is not included in the lactate dehydrogenase gene, as recited in the claims.

Accordingly, Applicant respectfully requests withdrawal of the § 112, second paragraph rejection.

IV. REJECTION UNDER 35 U.S.C. § 103(A)

The Office Action[1] maintained the rejection of claims 1-3, 6, 7 and 16-18 under 35 U.S.C. § 103(a) as being unpatentnable over WO 99/14335 to Porro et al. ("Porro"). Office Action at 7. Applicant respectfully traverses the rejection for at least the following reasons.

[1] The Office Action may contain a number of statements reflecting characterizations of the related art and the claims. Regardless of whether any such statement is identified herein, Applicant declines to automatically subscribe to any statement or characterization in the Office Action.

A. Clarification on the term in dispute

Applicant has previously argued that the claimed transformants provide unexpected benefits over the teachings of Porro and that the results obtained from the claimed transformants were not predictable in the prior art, corroborated by the Declaration of Mr. Toru Onishi under 37 C.F.R. § 1.132 ("Declaration"). *See* Reply to Office Action filed March 23, 2010, pages 8-10.

In response, the Office Action contended Applicant's arguments and Declaration insufficient to overcome the rejection. Specifically, the Office Action asserted that the lactic acid yields of the present application and Porro are "nearly identical," as shown in Table 1 of Declaration. Office Action at 4. Alleging that "in the field of fermentation, 'fermentation efficiency' can be viewed as an expression of how much product (e.g., lactic acid) was actually produced relative to the amount that could be theoretically produced," the Office Action further asserted that "the specification and [Declaration] do not specify the theoretical amount of lactic acid that is predicted to be produced by a given amount of glucose in a transformant having a [chromosomally]-integrated LDH gene." *Id.* pages 4-5 and 7-8.

Applicant respectfully submits that the expression "an increased efficiency" presented in Applicant's arguments and Declaration does not correspond to the term "fermentation efficiency" as relied on in the Office Action. The disputed expression "an increased efficiency" is used to point out that the lactic acid yield from the claimed transformant was much higher than the yield that could be predicted in the cited references, indicating that the claimed transformant is far more efficient in lactic acid production than the transformants disclosed in the cited references.

In the March 23, 2010 Reply, corroborated by the Declaration, Applicant argued that the claimed transformant produced unexpectedly large amount of lactic acid, as compared to the prior art. For example, in Porro, when the yeast transformant carrying multiple copies of an LDH gene was used, the lactic acid yield was 33.8%. *See* Table 1 of Declaration. The declaration also noted that the 2μm plasmid, as used in Porro's transformant, maintains 20-50 copies. *See* Declaration, paragraph 13. Considering these disclosures of Porro, one of ordinary skill in the art would recognize that the lactic acid yield attributable to each single copy of the LDH gene would be at most ~1.7% (=33.8%/20 copies). As compared to this lactic acid yield from a single copy predicted in Porro, the present application discloses much higher lactic acid yield from the claimed transformant containing a single copy of the LDH gene (32.8%).

B. Response to the Office Action's assertions based on Ishida

Further, the Office Action noted that "both columns 5 and 6 in Table 1 of Declaration [(Ishida et al.[2] ("Ishida") and the present application, respectively)] disclose a transformed *S. cerevisiae* having a bovine LDH gene integrated into its genome, and yet produce significantly different yields of lactic acid." Office Action, p. 5. The Office Action alleged that the yeast strains used in Ishida (YIBO-7A) and the present application (KCB-27) are different, and "even various *S. cerevisiae* can result in different yields of fermentation products." *Id.* Relying on the above allegations, the Office Action further asserted that "the asserted 'unexpected' high yield of the claimed invention may

[2] Ishida, N. et al., *Efficient production of L-Lactic acid by metabolically engineered* Saccharomyces cerevisiae *with a genome-integrated L-lactate dehydrogenase gene.* Appl. Environ. Microbiol. Vol. 71, No. 4, pp. 1964-1970 (2005).

not be solely due to a chromosomally-integrated LDH gene." *Id.* Applicant respectfully disagrees with these allegations.

The lactic acid yield disclosed in Ishida (62.2%) and the yield disclosed in the present application (32.8%) do not differ as widely as compared to the difference in lactic acid yields between the present application and the yield predicted in Porro (~1.7%), as discussed above. Notably, there is only a 2x difference between the present application and Ishida compared to almost a 20x difference between the present invention and Porro.

Further, Applicant respectfully directs the Examiner's attention to the following chart, comparing the experimental conditions disclosed in Ishida and the present application.

	Ishida (Ref. 3)	Present application
Transformant	Diploidization of haploid yeast cells each having a single insertion of bovine LDH gene, resulting in two copies of LDH genes in the transformant (*see e.g.*, Fig. 2; p.1967, left col., ll. 5-8)	only a single copy of bovine LDH gene incorporated into the transformant
Initial glucose amount	100 g/L (Fig. 3) mild osmotic pressure	150 g/L high osmotic pressure
Fermentation medium	50 g/L calcium carbonate (neutralizing agent) (Fig. 3)	No neutralizing agent (acidification is likely during fermentation)

In view of the above disclosures, Applicant submits that the yield disclosed in the present application (32.8%) lower than the yield disclosed in Ishida (62.2%) appears attributable to the fact that Ishida has double the copy number of the LDH gene when compared to the present application, and the relatively harsh experimental conditions in

terms of osmotic pressure to the transformants and the acidity of the medium, in the present application.

Accordingly, Applicant respectfully submits that the Office Action's above-noted allegations based on the experimental results from Ishida and the present application are improper.

C. Porro neither discloses nor suggests all of the features of the present claims

The Office Action further relied on claims 1, 16, and 19-21 of Porro, and asserted that Porro "explicitly claimed an embodiment of transformed yeast having a chromosomally-integrated LDH gene." Office Action at 8. Claims 1, 16, and 19-21 of Porro, however, neither disclose nor suggest all of the features of the present invention's claims 1 and 16. For example, Porro's claims do not disclose at least "wherein the pyruvate decarboxylase gene on the host chromosome is replaced with the single copy of the lactate dehydrogenase gene [incorporated into the host chromosome]," as presently claimed. Porro provides no reason or motivation to use a chromosomally-integrated transformant. Porro instead recognizes increased lactic acid production due to introducing multiple copies of an LDH gene to the cells, as previously argued in the May 23, 2010 Reply, page 10; Declaration, paragraph 17.

For at least the foregoing reasons and the reasons of record in the March 23, 2010 Reply, claims 1-3, 6, 7, and 16-18 should be allowable over WO 99/14335.

V. DOUBLE PATENTING REJECTION

The Office Action provisionally rejected claims 1-7 and 16-18 on the grounds of nonstatutory obviousness-type double patenting over claims 16-28 of co-pending Application No. 12/324,804. Office Action at 16-17. Since no claims are allowed in either of the relevant applications, the Applicant respectfully requests that the rejection

be held in abeyance until subject matter is allowed in either of the relevant applications. Applicant will file a Terminal Disclaimer once patentable subject matter is indicated by the Office Action, and if at that time the Office Action has not withdrawn the obviousness-type double patenting rejection. *See* M.P.E.P. § 804(I)(B).

VI. CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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